



# 4

# SEQUENCE LISTING

<110> Bowdish, Katherine S.  
Frederickson, Shana  
Renshaw, Mark

<120> RATIONALLY DESIGNED ANTIBODIES

<130> 1087-2

<140> 10/006,593

<141> 2001-12-05

<150> US 60/251,448

<151> 2000-12-05

<150> US 60/288,889

<151> 2001-05-04

<150> US 60/294,068

<151> 2001-05-29

<160> 118

<170> PatentIn version 3.1

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Gly Gly

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<213> human

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<210> 19  
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atc 63

<210> 24

<211> 63

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gtg 63

<210> 25  
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<220>  
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<400> 25  
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1 5 10 15

Gly Gly

<210> 26  
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<210> 27  
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<220>  
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<400> 27

Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala  
1 5 10 15

Gly Gly

<210> 28  
<211> 54  
<212> DNA  
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<220>  
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<400> 28  
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<210> 29  
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<400> 29

Gly Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala  
1 5 10 15

Gly Gly

<210> 30  
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 1 5 10 15

Pro Val

<210> 32  
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<210> 33  
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 1 5 10 15

Val Gly

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<400> 35

Val Val Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala  
1 5 10 15

Pro Val

<210> 36  
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<210> 37  
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Gly Pro Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala  
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Pro Asp

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<400> 39

Leu Pro Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala  
1 5 10 15

Pro Val

<210> 40  
<211> 54  
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Ser Leu Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala  
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Pro Ile

<210> 42  
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Pro Val

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Thr	Thr	Ile	Glu	Gly	Pro	Thr	Leu	Arg	Gln	Trp	Leu	Ala	Ala	Arg	Ala
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Pro Val

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<210> 47  
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Thr	Arg	Ile	Glu	Gly	Pro	Thr	Leu	Arg	Gln	Trp	Leu	Ala	Ala	Arg	Ala
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Cys Ser

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<400> 49

Gln	Thr	Ile	Glu	Gly	Pro	Thr	Leu	Arg	Gln	Trp	Leu	Ala	Ala	Arg	Ala
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Pro Asp



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 gaggaaaaag tgaaaaccct gaaagctcag aactccgagc tggcgtccac tgccaacatg 120  
 ctgcgcgaac aggtggcaca gctgaaacag aaagttatga accatggcgg ttgtgctagt 180  
 ggccaggccg gccagcacca tcaccatcac catggcgcgcat acccgtagca cgttccggac 240  
 tacgcttctt aggaggggtgg tggctctgag 270

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Pro Lys Pro Ser Thr Pro Pro Gly Ser Ser Cys Gly Gly Arg Ile Ala  
 1 5 10 15

Arg Leu Glu Glu Lys Val Lys Thr Leu Lys Ala Gln Asn Ser Glu Leu  
 20 25 30

Ala Ser Thr Ala Asn Met Leu Arg Glu Gln Val Ala Gln Leu Lys Gln  
 35 40 45

Lys Val Met Asn His Gly Gly Cys Ala Ser Gly Gln Ala Gly Gln His  
 50 55 60

His His His His His Gly Ala Tyr Pro Tyr Asp Val Pro Asp Tyr Ala  
 65 70 75 80

Ser

<210> 54  
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<400> 54

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gccctggac aagggcttga gtggatggga gggatcttcc ctttccgtaa tacagcaaag	180
tacgcacaac acttccaggg cagagtcacc attaccgcgg acgaatccac gggcacagcc	240
tacatggagc tgagcagcct gagatctgag gacacggcca tatattattg tgcgagaggg	300
gatacgattt ttggagtgac catgggatac tacgctatgg acgtctgggg ccaagggacc	360
acggtcaccg tctccgcagc ctccaccaag ggcccatcgg tcttccccct ggcaccctcc	420
tccaagagca cctctggggg cacagcggcc ctgggctgcc tgggtcaagga ctacttcccc	480
gaaccgggtga cggtgtcgtg gaactcaggc gccctgacca gcggcgtgca caccttcccc	540

gctgtcctac agtcctcagg actctactcc ctcagcagcg tggtgaccgt gccctccagc 600  
agcttgggca cccagaccta catctgcaac gtgaatcaca agcccagcaa caccaagggtg 660  
gacaagaaag ttgagcccaa atcttgtgac aaaactagt 699

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caggctccca ggctcctcat ctatggtaca tccagcaggg ccaactggcat cccagacagg 180  
ttcagtggca gtgggtctgg gacagacttc actctcacca tcagcagact ggagcctgaa 240  
gattttgcag tgtactactg tcagcagtat ggtggctcac cgtggttcgg ccaagggacc 300  
aaggtggaac tcaaacgaac tgtggctgca ccattctgtct tcatttccc gccatctgat 360  
gagcagttga aatctggaac tgcctctgtt gtgtgcctgc tgaataactt ctatcccaga 420  
gaggccaaag tacagtggaa ggtggataac gccctccaat cgggtaactc ccaggagagt 480  
gtcacagagc aggacagcaa ggacagcacc tacagcctca gcagcaccct gacgctgagc 540  
aaagcagact acgagaaaca caaagtctac gcctgcgaag tcacccatca gggcctgagc 600  
ttgcccgtca caaagagctt caacagggga gagtgttagt tctaga 646

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Leu Ala Ala Arg Ala Xaa Xaa Trp Gly Gln Gly Thr  
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<222> (64)..(65)

<223> n is a, c, g or t

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<223> n is a, c, g or t

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gcgnnyntt ggggccaagg gacc 84

<210> 58

<211> 60

<212> DNA

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<212> PRT

<213> artificial sequence.

<220>



<223> TPO mimetic with flanking amino acids

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Arg Gly

<210> 62

<211> 41

<212> DNA

<213> artificial sequence

<220>

<223> primer

<400> 62

taggatgcgg ccgcacaggt cttttttttt tttttttttt t 41

<210> 63

<211> 24

<212> DNA

<213> artificial sequence

<220>

<223> primer

<400> 63

ccatgtaggc tgtgcccgtg gatt 24

<210> 64

<211> 24

<212> DNA

<213> artificial sequence

<220>

<223> primer

<400> 64

ccacgggcac agcctacatg gagc 24

<210> 65

<211> 54

<212> DNA

<213> artificial sequence

<220>

<223> nucleic acid encoding TPO mimetic peptide flanking sequence

<400> 65

ttgcccaattg aagggccgac gctgcggcaa tggctggcgg cgcgcgcgcc tggt

54

<210> 66  
<211> 18  
<212> PRT  
<213> artificial sequence

<220>  
<223> TPO mimetic peptide with flanking sequence

<400> 66

Leu Pro Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala  
1 5 10 15

Pro Val

<210> 67  
<211> 472  
<212> PRT  
<213> artificial sequence

<220>  
<223> Humanized antibody heavy chain

<400> 67

Met Lys Trp Ser Trp Val Ile Leu Phe Leu Leu Ser Val Thr Ala Gly  
1 5 10 15

Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys  
20 25 30

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe  
35 40 45

Ser Asn Tyr Trp Ile Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu  
50 55 60

Glu Trp Met Gly Glu Ile Leu Pro Gly Ser Gly Ser Thr Glu Tyr Thr  
65 70 75 80

Glu Asn Phe Lys Asp Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser  
85 90 95

Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val  
100 105 110

Tyr Tyr Cys Ala Arg Leu Pro Ile Glu Gly Pro Thr Leu Arg Gln Trp  
 115 120 125

Leu Ala Ala Arg Ala Pro Val Trp Gly Gln Gly Thr Leu Val Thr Val  
 130 135 140

Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys  
 145 150 155 160

Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys  
 165 170 175

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu  
 180 185 190

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu  
 195 200 205

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr  
 210 215 220

Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val  
 225 230 235 240

Asp Lys Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro  
 245 250 255

Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro  
 260 265 270

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val  
 275 280 285

Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val  
 290 295 300

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln  
 305 310 315 320

Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln  
 325 330 335

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly  
 340 345 350

Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro  
 355 360 365

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr  
 370 375 380

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser  
 385 390 395 400

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr  
 405 410 415

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr  
 420 425 430

Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe  
 435 440 445

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys  
 450 455 460

Ser Leu Ser Leu Ser Leu Gly Lys  
 465 470

<210> 68

<211> 1419

<212> DNA

<213> artificial sequence

<220>

<223> nucleic acid encoding humanized antibody heavy chain

<400> 68

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tgtaaagcta gcggctatat tttttctaatt tattggattc aatgggtgog tcaggccccc	180
gggcagggcc tggaatggat gggtagatc ttaccgggct ctggtagcac cgaatatacc	240
gaaaatttta aagaccgtgt tactatgacg cgtgacactt cgactagtag agtatacatg	300
gagctctcca gcctgcgacg ggaggacacg gccgtctatt attgcgcgog tttgcccaatt	360

gaagggccga cgctgcggca atggctggcg gcgcgcgcgc ctgtttgggg tcaaggaacc 420  
 ctggtcactg tctcgagcgc ctccaccaag ggcccatccg tcttccccct ggcgccctgc 480  
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<210> 69  
 <211> 236  
 <212> PRT  
 <213> artificial sequence

<220>  
 <223> Humanized antibody light chain

<400> 69

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp  
 1 5 10 15

Leu Arg Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser  
 20 25 30

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Gly Ala Ser  
 35 40 45

Glu Asn Ile Tyr Gly Ala Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys  
 50 55 60

Ala Pro Lys Leu Leu Ile Tyr Gly Ala Thr Asn Leu Ala Asp Gly Val  
 65 70 75 80

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr  
 85 90 95

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Asn  
 100 105 110

Val Leu Asn Thr Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile  
 115 120 125

Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp  
 130 135 140

Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn  
 145 150 155 160

Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu  
 165 170 175

Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp  
 180 185 190

Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr  
 195 200 205

Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser  
 210 215 220

Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys  
 225 230 235

<210> 70  
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 gtcaccatca cctgcggcgc cagcgaaaac atctatggcg cgctgaactg gtatcaacag 180  
 aaacccggga aagctccgaa gcttctgatt tacggtgcca cgaacctggc agatggagtc 240  
 ccttctcgct tctctggatc cggctccgga acggatttca ctctgaccat cagcagtctg 300  
 cagcctgaag acttcgctac gtattactgt cagaacgttt taaatactcc gttgactttc 360  
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 ccgccatctg atgagcagtt gaaatctgga actgcctctg ttgtgtgcct gctgaataac 480  
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 tcccaggaga gtgtcacaga gcaggacagc aaggacagca cctacagcct cagcagcacc 600  
 ctgacgctga gcaaagcaga ctacgagaaa cacaaagtct acgcctgcga agtcacccat 660  
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 <212> PRT  
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 <222> (1)..(2)  
 <223> Xaa is any amino acid

<220>  
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 <222> (6)..(6)  
 <223> Xaa is any amino acid

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 <222> (15)..(15)  
 <223> Xaa is any amino acid

<220>

<221> MISC\_FEATURE  
 <222> (21)..(22)  
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<400> 71

Xaa Xaa Asp Tyr His Xaa Arg Met Gly Pro Leu Thr Trp Val Xaa Lys  
 1 5 10 15

Pro Leu Gly Gly Xaa Xaa  
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<210> 72  
 <211> 21  
 <212> DNA  
 <213> artificial sequence

<220>  
 <223> primer

<400> 72  
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<210> 73  
 <211> 39  
 <212> DNA  
 <213> artificial sequence

<220>  
 <223> primer

<400> 73  
 cacgcgcaca acacgtctag araccatccag atgaccccag 39

<210> 74  
 <211> 39  
 <212> DNA  
 <213> artificial sequence

<220>  
 <223> primer

<400> 74  
 cacgcgcaca acacgtctag agmcatccag ttgaccccag 39

<210> 75  
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 <212> DNA  
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<223> primer

<400> 75

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39

<210> 76

<211> 39

<212> DNA

<213> artificial sequence

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<223> primer

<400> 76

cacgcgcaca acacgtctag agtcattctgg atgacccag

39

<210> 77

<211> 39

<212> DNA

<213> artificial sequence

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<223> primer

<400> 77

cacgcgcaca acacgtctag agatattgtg atgacccag

39

<210> 78

<211> 39

<212> DNA

<213> artificial sequence

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<223> primer

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<212> DNA

<213> artificial sequence

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<223> primer

<400> 79

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<210> 80

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<223> primer

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<210> 81

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<213> artificial sequence

<220>

<223> primer

<400> 81

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<210> 82

<211> 39

<212> DNA

<213> artificial sequence

<220>

<223> primer

<400> 82

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39

<210> 83

<211> 39

<212> DNA

<213> artificial sequence

<220>

<223> primer

<400> 83

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<210> 84

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<212> DNA

<213> artificial sequence

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<223> primer

<400> 84

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39

<210> 85  
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 <223> primer  
  
 <400> 85  
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 <212> DNA  
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 <400> 86  
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 <210> 87  
 <211> 20  
 <212> DNA  
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 <220>  
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 <400> 87  
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 <210> 88  
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 <400> 88  
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 <223> primer  
  
 <400> 89

agccagccac tggcgcaggg ttgggccttc gatcggggtt tgaataatga aaatagcag 59

<210> 90  
<211> 59  
<212> DNA  
<213> artificial sequence

<220>  
<223> primer

<400> 90  
agccagccac tggcgcaggg ttgggccttc gatcggggtt taaatgagca rcttaggag 59

<210> 91  
<211> 59  
<212> DNA  
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<220>  
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Gln Gly

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 gggaaagctc ctaagctcct gatctataac ccgatcgaag gcccaaccct gcgccagtgg 180  
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Ser Ser Val Lys Val Ser Cys Arg Ala Ser Gly Gly Thr Phe Asn Asn  
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Tyr Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp  
 35 40 45

Met Gly Gly Ile Phe Pro Phe Arg Asn Thr Ala Lys Tyr Ala Gln His  
 50 55 60

Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Gly Thr Ala  
 65 70 75 80

Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Ile Tyr Tyr  
 85 90 95

Cys Ala Arg Gly Asp Thr Ile Phe Gly Val Thr Met Gly Tyr Tyr Ala  
 100 105 110

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ala Ala Ser  
 115 120 125

Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr  
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Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro  
 145 150 155 160

Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val  
 165 170 175

His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser  
 180 185 190

Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile  
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Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val  
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Glu Pro Lys Ser Cys Asp Lys Thr Ser  
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 35 40 45

Gly Thr Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser  
 50 55 60

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu  
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Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Gly Ser Pro Trp Phe  
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Gly Gln Gly Thr Lys Val Glu Leu Lys Arg Thr Val Ala Ala Pro Ser  
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Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala  
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Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser  
145 150 155 160

Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr  
165 170 175

Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys  
180 185 190

Glu Val Thr His Gln Gly Leu Ser Leu Pro Val Thr Lys Ser Phe Asn  
195 200 205

Arg Gly Glu Cys  
210